individually perfect themselves in the management of all these four phases of childhood, and this leads me to the final consideration in the development of the practice of pediatrics to which I wish to call your attention and toward which I believe modern pediatrics is tending, that is the association of a group of specially qualified pediatricians who will together cover these various phases of the field of pediatrics.

Today many groups in medicine are being formed throughout this country. These groups usually consist of an internist, surgical specialists of various types, laboratory, X-ray, and the most successful groups are closely affiliated with some hospital. In some of these groups the pediatrician is included but usually not. The pediatrician is, I believe, the center around which the best group for the care of the whole period of childhood, including adolescence, must develop in the future. With a group of pediatricians in any large city must be associated the specialists who are particularly trained to care for the type of specialty work (surgery, nose and throat, dentistry, etc.) related to these periods of child life. Such a group should not only be interested in the cure of disease, but should also interest itself in the preventive side of infant and child welfare. This should include not only the physical but also the mental, psychological and psychiatric aspects of childhood. Without such a broad and comprehensive vision of the field of pediatrics I feel that our development will not be as healthy and well rounded as it should be. The work of such a group must be carried on in connection with a children's hospital or children's department in a general hospital where all the facilities for the study of special cases are available and where a broad and comprehensive opinion for the management and treatment of cases is possible. It may be satisfactory to treat a large percentage of cases in an office practice, but it is almost impossible to arrive at any well rounded conclusion regarding many of these cases without a period of thorough observation and investigation in a hospital. Such an observation period may cover a few days or several weeks, but during this time every phase of the child's condition should be studied. As a group pediatricians are not only interested in the cure of disease and of abnormal conditions that may lead to disease or to a handicapped life either mental or physical, but must learn to consider a child as a whole—body, mind and soul—and it is for this complex relationship that we are looked to more and more each day, not only to diagnose a diseased condition but to advise and guide as to a child with its parents and guardians through the difficult adjustments that many growing individuals have to make.

THE TREATMENT OF TUBERCULOSIS WITH PARTIGENS (AFTER MUCH-DEYCKE)*

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1. What are Partigens?
2. Scientific foundation for the justification of this method of treatment.
   (a) Immunity in tuberculosis in general.
   (b) Biological tests (in regard to the effect of partigens).
   (c) Cellular and humoral immunity.
3. In what respects do partigens differ, regarding their effect, from the tuberculins which are on the market and in use today?
4. Demonstration of diapositives, showing cases treated with partigens.

The problems met in the creation of a treatment which has for its object the cure by immunization are, first: To establish the fact, that the natural defense of the body consists in the production of immune bodies against the infection. Second: Admitting the quantity to be sufficient to overcome the infection, whether they confer immunity for future attacks of the same character. Third: To estimate in what, or by what tissues these immunizing agents are formed. And, fourth: If they can be transferred to another individual and grant immunity.

These facts are well established for certain infections, for example, diphtheria.

In the treatment of tuberculosis they represent the foundations, on which Much of Hamburg based his research work with his so-called "partial antigens."

What are partial antigens, or, as they are called for short, "partigens"?

They are prepared from tubercle bacilli in the following manner: Cultures are carefully broken up with physiological salt solution, containing one-half per cent lactic acid; this suspension is incubated at 65° C., until the acid-fastness of the bacilli has entirely disappeared, and until it is no longer possible, to stain even Much's granula (after the method of Gram-Much).

This disintegrated substance, which is called M. Tb., is filtered.

The water-soluble part, containing the toxin of the tubercle bacilli, and representing the pure tuberculin, is called L.

The residuum, non-soluble in water, is called M. Tb. R. This again is treated with alcohol and ether, and the three end products are called the partial antigens—first, the fatty-acid-lipoids, soluble in alcohol, are called F.; second, the neutral fats and highly molecular fats, soluble in ether, called N.; third, an entirely non-soluble residuum, of a highly albumenous content, containing a large amount of phosphorous and belonging, most probably, to the group of nucleo-proteids, called A.

These are the three partial antigens, and are those that are used for treatment, while the pure tuberculin, L., is not used at all, or only in exceptional cases.

Much and his school teach: "A cure of tubercu-

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losis is impossible without creation of an absolute immunity." The proof of this statement is demonstrated by animal experiments and by the observation of larger groups of people, or whole nations.

Behring was the first to show that an immunization for tuberculosis is possible. He vaccinated cattle with human tubercle bacilli and immunized them (even if only for a certain period) against tuberculosis. This fact has been definitely established. Much and Deycke succeeded in producing an immunization with substances derived from dead tubercle bacilli, which we have never been able to do with the tuberculins, that we have been using up to the present time.

Koch was the first to demonstrate, that an infection with tubercle bacilli protects animals against a second infection. Roemer corroborated Koch's deductions and proved, that the protection thus granted was very stable. To use his own words, "In spite of the fact that an animal might be tuberculous, it is tuberculosis-immune against a second infection." The original infection might at the same time progress or become arrested. This assertion found a great deal of contradiction in the beginning, because the quantitative values and the conditions of time, which are of the greatest importance, were not properly considered by the workers, who checked up these experiments.

The observations of localities, or countries, which have been practically free from tuberculosis, furnish further interesting and valuable data. The fact in itself, that an infection is of long duration, presupposes extensive processes of immunization, and the difference between an acute and a chronic illness is based on the amount of defense and immunity developed. Much, Deycke, Wolff-Eisner, and others proved by their observations in Palestine, Turkey, the Argentines, Africa and other countries, that tuberculosis is not universally always a chronic disease. It can become pandemic, just like any other plague, when it invades a country which has been free from tuberculosis, and whose inhabitants have not been able to acquire previously a certain degree of immunity. The explanation of these facts teaches: People who live in a country, where tuberculosis is a common disease, and who have, therefore, been infected at sometime with tubercle bacilli, are protected against the disease. People who have never been infected, are not protected and succumb. "Contact with tuberculosis leads to immunity, lack of contact means lack of protection."

In practically all cases which are suffering from tuberculosis, antibodies can be demonstrated in the blood. But all attempts to influence tuberculosis with derivatives of blood of animals or human beings, previously treated, have been without results. The reason for this failure is explained in the following way: To be complete for immunizing purposes a serum, or any other blood preparation, must contain all the partial antibodies. This we have not been able to obtain so far, but even if it were possible to prepare such a product, its success would not be assured, as the humoral elements play an insignificant role in immunity against tuberculosis. The cellular immunity has been found to be the most important feature in the immunization process.

Much and Leschke published the following animal experiments:

1. Goats were treated with the three partial antigens. They developed in their blood all the necessary antibodies; at this time the blood-plasma of these goats possessed definite protective qualities for other animals. Later the antibodies disappeared entirely, or partially, and the blood did not provide any further protection to other animals; but the goats themselves proved entirely immune to an inoculation with tubercle bacilli.

2. Blood-plasma of a human being, immune to tuberculosis, was mixed at different times with 5 mg. tubercle bacilli and injected intraperitoneally into guinea pigs. The plasma was previously examined for partial antibodies. If none or only part of these were present in the plasma, the animals died rapidly from extensive tuberculosis. But, if all the partial antibodies were present in the plasma, it showed an astonishing immunizing quality, and the animals did not develop tuberculosis, in spite of the enormous dosages of bacilli.

These experiments furnish a most valuable support for the treatment with partial antigens.

Much and his school proved by the first of these experiments, that the cellular immunity plays a far more important role in tuberculosis than the humoral immunity. They demonstrate the cellular immunity with the help of the skin-test, the humoral by complement fixation.

Their biological tests have thrown an interesting light on the phenomena of cellular immunity. They proved again and again, by graduated intracutaneous reactions and complement fixation tests, that in many cases of tuberculosis no antibodies are found in the serum, in spite of very strong skin reactions. They showed further, that the quantities of antibodies in the serum are most changeable, but that the reactivity of the cells of the skin remains the same over a long period of time.

Much sums up the question of immunity in the following manner:

"Immunity in tuberculosis consists of two kinds: a humoral and a cellular. For the defense against an infection the humoral immunity is absolutely necessary, for the continuation of the condition of immunity only the cellular is needed. If a second infection occurs in a being which has none or only some of the partial antibodies in the blood, but which possesses cellular immunity, the virus is overcome, because the cells dispatch partial antibodies into the blood current. The appearance of the sum of the partial antibodies after a renewed infection of an immunized being has been demonstrated in the human being as well as by animal experiments. After the new infection has again been overcome, a part, or all of the partial antibodies disappear from the blood, and only the cellular immunity persists."

With complement fixation only the humoral immunity is demonstrated; with the oversensitiveness reaction of the skin the humoral as well as

the cellular immunity is proven. For the fight itself the humoral immune-substances are necessary, for the defense the cellular ones are sufficient. The cellular immunity is the most necessary and important one.

These experiments, considerations, and their deductions, which can be here only superficially discussed, present the foundation of the treatment with the partial antigens of Much and his co-worker, George Deycke.

A comparison between these partial antigens and the tuberculins, which have been on the market up to the present time, presents interesting and rather important differences.

First of all we have to admit that the tuberculins have not fulfilled our expectations.

While they are entitled to credit under certain conditions and have many enthusiastic advocates, they have an equal number of decided opponents. Their failure as a universal specific is evidenced by the many preparations of tuberculins on the market, extravagant claims being made for all. With any one of the dependable preparations good results might be obtained in certain cases; with none of them can failures be avoided. We all have observed cases in which one form of tuberculin had no effect whatsoever and even seemed to be harmful to the patient, while a different preparation produced good results, and it has been impossible to explain this fact.

Why have the tuberculins, which we have been using up to the present time, failed to meet our expectations?

Principally, on account of their chemical composition. They all contain variable partial antigens, even if only in inconsiderable amounts. Besides the three partial antigens, which are non-soluble in water (albumen, fat-lipoid, neutral fat), they contain a special toxin and an aromatic substance. All these substances possess strongly reacting qualities. The reaction to pure tuberculin, or the pure toxin, is based on oversensitiveness to the toxin and is harmful, as has been proven by Much and his school.

The reaction to the other partial antigens is based on oversensitiveness to immunizing substances and is useful.

The tuberculins now offered on the market, for treatment, contain undetermined amounts of antigens, which makes their use very unscientific and inaccurate, and gives no aid in solving the complex problem of immunity. Normal animals cannot be immunized against tuberculosis by any of these tuberculins. There must either be some substance missing for the purpose of immunization, or it must be present in some combination which cannot be used. Undisintegrated bacillary substances do not produce all antibodies, and least of all those reacting particularly to fats. The normal body is unable to do the necessary work of disintegrating the bacillary substances contained in the old as well as the new tuberculin. Frequently one or the other partial antigen might be present in such a form that it could be used and then, if the system happens to have the other antibodies present for defense, the whole sum of partial antibodies might be formed and the treatment would be successful. This, however, is not the case in the great majority of patients, and would be only a coincidence, should these conditions be present.

In treating tuberculosis with partial antigens, however, all the antigens which are needed for treatment are injected in such a form that the body is able to produce antibodies for each one of them.

A radical difference between the tuberculins and the partigens, lies in the fact that the pure toxin of the bacilli is entirely removed in the treatment with partigens. This accounts for the absence of general reactions, which is so commonly seen when using the ordinary tuberculins, temporarily contraindicating their further use. On the other hand the partigens, being devoid of toxicity, can be used while the patient has febrile periods. A possible temperature of the patient during the treatment is not a result of the use of partigens, but it is due to the disease itself, or of one of its many complications. The correctness of this statement is proven by the fact that in fever cases the temperature frequently becomes normal during the treatment. The partigens can and usually do produce slight focal reactions, not severe ones, but no general reactions or fever. The first indication that the respective patient has reached the maximum dose of partigen is evidenced by a slight local reaction at the site of injection, a slight elevation of temperature following the injection. The only contraindications for the treatment with partigens are pulmonary hemorrhages, and an entirely negative reaction to all the skin tests with the different antigens. In this event other methods will have to be used (non-specific ones) to create first some reactivity in the patient, if this can be established at all.

Another important advantage in favor of the use of partial antigens lies in the fact that we are able to get a good picture of the status of immunity of the patient.

The injections for the demonstration of the status of immunity are made intracutaneously. They are based on the biological law of oversensitiveness. The result of this intracutaneous inoculation indicates which partial antigens should be used in the respective case. If we find, for instance, that the fatty-acid antibodies are missing and the antibodies for the albuminous and neutral-fat group are present, then the patients are treated advantageously with the fatty-acid antigen, F, and so on. With the skin-test we are able to ascertain whether antibodies are present, and, if they are present in large or small quantities, but we cannot determine if they are present in sufficiently large quantities to ward off the attack. In other words, we can measure the defense, but we cannot measure the attack. A patient might have a great many antibodies, and yet the number of these antibodies present would not be sufficient for defense against the infection, should the infection be an exceptionally virulent or massive one.

It is evident that if these claims, as they are made by Much and Deycke in favor of their partial antigens, should prove to be correct, a very acceptable advance will have been reached in the specific treatment of tuberculosis.